Ordering Genetic Tests and Reporting Results: Communication is Key

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Abstract/Introduction

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Context: Effective and accurate communication among health care providers, laboratory professionals and the public is essential for genetic testing to achieve its potential for improving health. Genetic tests must be used appropriately for a given situation to realize measurable health benefits. Over 1000 genetic tests are now available, with several reaching prominent clinical and public health significance. As this trend continues, concerns are raised about how genetic tests are ordered and results reported.

Objective: A project was launched to systematically evaluate practices associated with genetic test ordering and result reporting within the health care community.

Methods: We chose to look at DNA-based testing for cystic fibrosis (CF) as the model to assess laboratory practices associated with ordering of tests and reporting of results. Twenty six laboratories representing diverse geographic and practice settings were presented mock clinical scenarios by way of their native requisition form together with a genotypic result and asked to provide a test result report. Additional practice data not apparent from analysis of requisitions and reports were collected by way of a separate survey. Input from the laboratory and clinical provider communities was critical in developing an approach to analyzing the data collected.

Results: Several elements of variability were identified with the greatest being inconsistencies in how genotypic test results were reported, limitations of the test described, and collection/use of information provided on the requisition form. Items likely pertinent to compromising an accurate and comprehensible interpretation were identified.

Conclusion: These results support the need for consensus development in the areas of terminology and communication practices of specific elements often found on genetic test result reports.

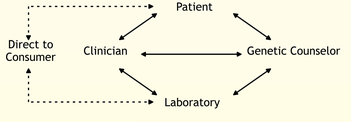
A Role for Public Health?

Assuring accurate information is effectively communicated to support informed decision making

Who is affected?

The family  The individual  The community 

The Testing Process



What is communicated? | What should be communicated?

Our Initial Focus: The Clinical Practice/Laboratory Interface

Health Care Providers ⟷ Laboratory

What are the questions?

For diagnostic tests:	How does the result correlate with the suspected diagnosis?
For carrier/ risk factor tests:	What do test results tell us about risk for disease? (to the patient or future children)

There are also implications beyond the patient

1. Other family members may be at risk or stigmatized
2. Community perception about genetic test results

What critical information should be communicated?

Before the test:

1. What test is requested
2. Why the test is requested
3. Relevant patient, family history, and partner information

After the test:

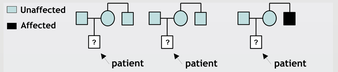
1. The test result
2. Interpretation in terms of the reason the test was ordered
3. Limitations in the use of the test result and interpretation
4. Implications for other family members, when appropriate
5. Follow up actions, as appropriate (i.e., genetic counseling)

Cystic Fibrosis: a Useful Model

- Life-shortening autosomal recessive disease
- Single gene disorder
- Affects multiple organ systems (pulmonary, gastrointestinal, pancreatic, etc.)
- Disease-associated mutations vary among ethnic/racial groups
- DNA-based testing is useful for diagnosis, carrier and newborn testing
- It is estimated that > 1,000,000 carrier tests are performed annually
- First DNA-based test recommended for population-based carrier screening for pregnant women or couples contemplating pregnancy

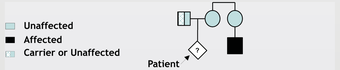
Interpreting Diagnostic Test Results: Rule In or Rule Out?

Model: Autosomal Recessive Disease; Two disease-associated alleles required



Disease-associated mutations found	2	1 or none	1 or none
Family History	None	None	Yes - Uncle affected
Interpretation	Correlates with disease	Does not rule out	Does not rule out
Chance of having an undetected mutation	Not relevant (caveat: different chromosomes?)	Need to know detection rate for panel and race/ethnicity	Need to know family-specific mutation and/or detection rate for panel and race/ethnicity

Interpreting Carrier Test Results: Determining Risk



A priori data			
Race/ethnicity population-based risk (for being a carrier)	Caucasian 1 in 29	African American 1 in 65	Ashkenazi Jewish 1 in 29
What is the risk of offspring having CF if:			
One partner carrier/ testing not performed for partner/ first cousin affected	1 in 8	1 in 8	1 in 8
One partner carrier/ testing not performed for other partner/ no family history	1 in 116	1 in 260	1 in 116
One partner carrier/ one partner negative / no family history	1 in 560	1 in 828	1 in 3,720

Testing performed using recommended panel: Genetics in Medicine, March/April 2001, Vol. 3 No. 2: 149-154

Variability in Test Reports for DNA based Cystic Fibrosis and Factor V Leiden in North American Laboratories

2000-2003: A CDC / Tulane University Schools of Public Health and Medicine collaboration

First Study: Evaluating the variability in Test result reports

Demographics of Laboratories Performing Molecular Cystic Fibrosis and Factor V Leiden Tests

Test/laboratory type (n)	No. (%) responding	US/Canadian
Cystic fibrosis		
Academic (28)	16 (57)	24 / 4
Hospital-based (8)	5 (63)	4 / 4
Independent (8)	7 (88)	7 / 0
Total = 44	28 (64)	
Factor V Leiden		
Academic (41)	21 (51)	39 / 2
Hospital-based (15)	13 (87)	10 / 5
Independent (16)	12 (75)	16 / 0
Total = 72	46 (64)	

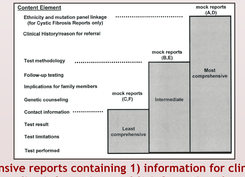
Percentage of Laboratories including Specified Elements within their Result Reports

	Cystic fibrosis (N=28) (%)	Factor V Leiden (N=46) (%)	CLIAC/NCCLS recommended
Administrative elements			
Specimen collection date	46	63	Yes
Contact info	86	87	Yes
Patient-specific elements			Yes
Clinical indication	64	39	Yes
Ethnicity listed	21	NA	Yes
Gender listed	46	46	Yes
DOB listed	79	80	Yes
Test-specific elements			Yes
Interpretation	93	96	Yes
Mutations listed	96	NA	Yes
Detection rate	86	NA	Yes
Post-test-specific elements			
Adjusted risk	71	NA	Yes
Genetic Counseling	61	52	Yes

Findings: There is variability in content of CF and fV Leiden DNA-based test reports

Physicians' Perceived Usefulness of and Satisfaction with Test Reports for Cystic Fibrosis and Factor V Leiden

Second Study: We distributed three mock reports of varying complexity for CF (A, B, C) and fV Leiden (D, E, F) to general and specialty physicians for their evaluation of usefulness and satisfaction.



Findings: Comprehensive reports containing 1) information for clinical decision making, 2) genetic counseling information, and 3) information about family implications were perceived as most useful.

Krousel-Wood et. al. Andersson et. al. Genet Med 2003:5:166

A Time for Community Involvement: A National Forum

May 2-3, 2003

COMMUNICATION: Key to Appropriate Genetic Test Referral, Result Reporting and Interpretation

Objectives:

- Explore the challenge of communication among professionals involved in the genetic testing process
- Develop a plan for identifying problem areas and best practices

Outcomes:

1. Reports need to be comprehensive, consistent in format and content, and understandable to all members of the health care team. This has not been achieved.
2. There is a need to collect and analyze data to identify problems that potentially impact on patient outcomes.

Current Efforts: Assessing Current Practices: The Process

Engage Partners → Collect Laboratory Requisitions → Fill out and return requisitions to Laboratories → Collect Laboratory Test Reports (genotype provided) → Analyze requisitions and reports

2003-2004 | 2004 | 2005

Survey to gather additional data → National activity to identify best practices and develop implementation and evaluation plans

2005 / 2006

Cystic Fibrosis Case Studies Used to Challenge Laboratories and Clinicians

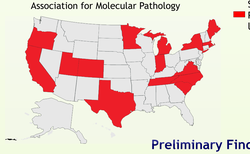
Indication for Testing	*Ethnicity*	*Family history*	*Mutation (provided)*
Diagnostic Testing			
Clinical suspicion	Caucasian	No	F508del/F508del
Clinical suspicion	Hispanic	No	3849+10kb C>T
Carrier Testing			
Partner is pregnant/carrier	Eurasian	Not available	R117H 5T/7T
Pregnant	African American	Yes-- Uncle affected	No mutations found
Pregnant	Caucasian	No	No mutations found

The Assessment: Who is Involved?

Organizers

Centers for Disease Control and Prevention
Wadsworth Center, NY Department of Health
Mt. Sinai School of Medicine
Association for Molecular Pathology

Genetic Testing Laboratories Participating



Participating laboratory settings (32 total)

Private	13 (41%)
Academic	16 (50%)
Large Reference	3 (9%)

Clinical Providers Participating (as advisors)

1. Pediatricians
2. OB-GYNs
3. Genetic Counselors
4. Nurse Practitioners
5. Family Practice Physicians
6. Physician Assistants
7. CF Center Directors

Preliminary Findings: An Example

Detection Rate: The likelihood of detecting a mutation if present for the methodology used

Detection rate can vary among laboratories because:
1. The methodology can differ (chosen by lab by what is available and most appropriate)
2. There is variation in the categories chosen to describe the patient's ethnicity/race
3. There is variation in the method used to collect family history information

Choice provided for selecting a patient's ethnicity/race

Choices available	# laboratories (32 total)
Nondirective	8 (25%)
3-4 Descriptors	4 (12%)
5 Descriptors	6 (19%)
14 Descriptors	14 (44%)

How family history is collected

Some choices available	# laboratories (32 total)
Specifically asks if there is a family history	19 (59%)
Test results for other family members	7 (22%)
Requests pedigree	8 (25%)

Implication: for the same patient (and methodology) laboratory detection rates can differ resulting in variation in diagnostic sensitivity and risk estimates

Preliminary Summary of Findings and Issues under Investigation

- Best practices have not been identified for effectively communicating the results and limitations of genetic tests
  Implication: Confusion and inconsistency in use of genetic tests
- Variability exists in both how patient- and family- specific information is collected and used for ordering CF tests and reporting results
  Implication: Clinical decisions or counseling based upon incomplete or inaccurate information
- Selection and use of a patient's race/ethnicity varies among laboratories and incidence/prevalence data is not well represented in the peer-reviewed literature.
  Implication: Risk estimates can vary depending what data is used

Next Steps

- Complete detailed analysis of test requisition and result reports
- Engage clinical, public health, and laboratory communities to identify best practices
- Implement and evaluate recommendations

Public Health Significance

As of January 2005, > 1000 genetic tests are listed as available on the Gene-Tests website(http://www.genetests.org).

As such testing becomes integrated into both clinical and public health programs, it is crucial to establish best practices in effectively communicating about genetic tests to assure best patient and population outcomes.